# Response to "Radiation Therapeutic Gain and Asian Botanicals," by Stephen Sagar

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## Abstract

Numerous botanical agents, many of which are used in whole medical system practices (i.e. traditional Chinese medicine, Ayurvedic medicine, etc.), have been shown to exhibit radiomodifying effects on tumors and normal tissues in-vitro and in-vivo studies. Some of these agents can enhance the therapeutic gain of radiation therapy by either acting as a radiosensitizer to tumor cells and/or as a radioprotector to normal cells. Botanical agents are comprised of multiple phytochemical compounds that may work individually or synergistically to not only improve radiation therapy outcomes, but may also exhibit a variety of anti-cancer effects as well. It will be important to evaluate these botanicals for efficacy, tumor specificity, and safety profiles before they can be recommended during radiation therapy.

## Keywords

radiomodifying, herbal medicine, antitumor, side effects, interactions

The use of nontoxic, inexpensive botanical agents to cause a radiomodifying response to enhance therapeutic gain (ie, radiosensitization of tumors and/or radioprotection of normal tissues) is compelling. In his article published in this issue, "Can the Therapeutic Gain of Radiotherapy be Increased by Concurrent Administration of Asian Botanicals?", Dr. Stephen Stepehen Sagar addresses the data, mechanisms of action, and rationale supporting the use of botanical agents in radiation therapy.[1] Unfortunately, the literature is very limited in the number and quality, particularly in humans, of experiments that have attempted to address this approach. Theoretical mechanisms of action for enhancing the therapeutic gain are many (ie, preferential uptake of antioxidant molecules into normal tissues vs tumor tissues, decreased intratumoral DNA repair, decreased intratumoral production of endogenous antioxidants, inhibition of the cell cycle in radiosensitive phases, etc). In addition to their radiomodifying effects, some botanical agents have also been shown to exhibit nonradiomodifying antitumor effects such as upregulating immune modulating cytokines (ie, *Panax ginseng*,[2] etc), promoting apoptosis (ie, ginger extracts[3,4]), and inhibiting angiogenesis (ie, EGCG,[5] curcumin,[6,7] etc). Taking advantage of multiple antitumor mechanisms using botanical agents during radiation therapy is not dissimilar to conventional pharmacologic approaches that have similarly employed multiple chemotherapeutic, biologic, and/or immune modulating agents during radiation therapy. The theoretical advantages of botanical agents over conventional agents are their potentially lower side-effect profiles and significantly lower cost.

In addition to their antitumor effects, botanical agents have also been employed to help mitigate untoward side effects frequently encountered in oncology. Fatigue is one of the most common complaints in patients during and after chemotherapy and/or radiation therapy. Barton et al[9] recently published the findings of a phase 3 study that found that ginseng (*Panax quinquefolius*) seemed to exhibit positive effects in helping relieve cancer-related fatigue. Numerous other antitumor botanical compounds have also shown promise in relieving commonly experienced symptoms in oncology (ie, ginger, *Zingiber officinale*, has recently been reported to help reduce chemotherapy-induced nausea,[10] etc).

As discussed by Sagar, it is important that well-designed and rigorously conducted studies are undertaken to further investigate a wide range of questions that have yet to be answered: elucidating the various mechanisms of action, doses, routes of administration, effects of combination therapies, toxicity profiles, whole compound versus isolated

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bioactive agent, and so on. One of the primary concerns of oncologists is that of interaction of botanical substances with conventional therapies. It is critical that experiments are conducted to define whether specific botanical compounds reduce the efficacy of conventional treatments or increase toxicity. Furthermore, standardized production of quality botanical compounds is imperative in assuring that the ingredients, amount, and activity are the same in each dose administered.

## What Should We Recommend to Our Patients Now?

The lack of rigorously conducted studies examining the effects of botanicals during radiation therapy is a significant problem for oncologists. Primum non nocere is the "golden rule" that we all learned in medical school and is the conservative and safe approach to most therapies that are considered prior to recommending them to our patients. I highly encourage my patients to first discuss with me any supplemental, isolated botanical compounds that they might be considering taking so that we can review the latest data available. Increasingly, well-conducted studies are being reported to help us better understand these complex questions.

In general, consuming whole foods that contain the botanical compounds of interest are likely safe and theoretically may be more effective than the isolated extracts taken as a high-dose supplement. Thousands of phytochemical compounds have been identified that exhibit numerous anticancer effects on tumor cells and their microenvironment. A currently popular hypothesis, and one that I believe, is that by consuming a diet consisting of foods that contain a variety of phytochemicals, individuals may be able to make their body less conducive to tumor development, growth, and progression by acting on many anticancer pathways. Combining a whole foods anticancer approach concurrently with radiation therapy is one that I encourage in my patients.

### Author's Note

The views expressed in this article are those of the author and do not reflect the official policy or position of the Department of the Navy, Department of Defense, or the US Government.

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